

Amendments to the Specification:

Please amend the paragraph under the "**CROSS REFERENCE TO RELATED APPLICATIONS**" added in the first Preliminary Amendment dated January 8, 2002, as follows:

[00001.1] This application claims priority to U.S. Provisional Patent Application Serial No. 60/240,397, filed October 14, 2000, ~~and is related to U.S. Provisional Patent Application Serial No 60/282,831, filed April 10, 2001, U.S. Patent Application Serial No. 09/861,292, filed May 18, 2001, and U.S. Provisional Patent Application Serial No. 60/293,259, filed May 22, 2001, and is a continuation-in-part of U.S. Patent Application Serial No. 09/861,292, filed May 18, 2001,~~ all of which are incorporated herein by reference.

Please replace paragraph [00140] with the following amended paragraph:

[00140] The resulting data is reported as Median Fluorescence Intensity(MFI) per bead for both sets. Figure 12 shows the 3D surface map graphical results of the data collected in the 98 bead master mix experiment. The Y axis represents the molecular recognition sequence and the X axis represents the tagging sequence. Figure 13 shows the 3D surface map graphical results of the data collected in the 50 bead master mix experiment.

**Table 1**  
**50 Bead Molecular recognition sequences (Y= iso-G ~~iso-C~~ and X = iso-C ~~iso-G~~)**

Bead No.	Molecular recognition sequence	Seq Id No:	Bead No.	Molecular recognition sequence	Seq Id No:
1	GAXGTXTGTC	1	26	CXTCGCXTAC	26
2	CXGTTXTTCC	2	27	GXCXAAAAXG	27
3	GGXTTGXTAG	3	28	CXXGACXATC	28
4	CTTXGXTCTC	4	29	CCATXAGXCC	29
5	CXTCAXGAAC	5	30	GGCAXTXTGG	30
6	GTAGXTAXGC	6	31	CTXAACXGGG	31
7	GGAXGXTAAC	7	32	GGAXACGXG	32
8	CXGTATXGTG	8	33	GCGXTTAXG	33
9	CATXGGTAXG	9	34	GAGXAGXTXC	34
10	GATTXTCGXC	10	35	GXCTAAXCCG	35
11	GTTXAXGACC	11	36	GCXTGTXCAC	36
12	CXGAAXGATC	12	37	GXCAGAXTCG	37
13	CAAXTACGXC	13	38	CGTXCTAGXG	38
14	CGGXATAXAC	14	39	CGXXTAGTXG	39
15	GXAAAXXAGG	15	40	CXAGGXAACC	40
16	GTCXTAGXXC	16	41	CXAGAXGAXG	41
17	GXCCTXTAXC	17	42	CGXTGXGTC	42
18	CCXACXTGAG	18	43	CAGXCGTXAG	43
19	CTXXCAXAGG	19	44	GGCTXTGXAC	44
20	GTXGAXATGC	20	45	CCAGXGXAAG	45
21	GAAAXTGXXG	21	46	GGCXAATXGC	46
22	GCTGXAXATC	22	47	GXCTGCXGG	47
23	CGCAXATXAC	23	48	GAXCTXCGGC	48
24	CTGGXTCXAG	24	49	GTXCGAXGGG	49
25	GGAAXAXXCC	25	50	GGXXATCCXG	50

**Table 2**  
**98 Bead Molecular recognition sequences (Y= iso-G ~~iso-C~~ and X = iso-C ~~iso-G~~)**

Bead No.	Molecular recognition sequence	Seq Id No:	Bead No.	Molecular recognition sequence	Seq Id No:
1	GAXGTXTGTC	1	50	CCXXATGTXG	67
2	CXGTTXTTCC	2	51	GAGXAGXTXC	34
3	GGXTTGXTAG	3	52	GXCTAAXCCG	35
4	CTTXGXTCTC	4	53	GCXTGTXCAC	36
5	CXTCAXGAAC	5	54	GXCAGAXTCG	37
6	GXCTTCXATG	51	55	CGTXCTAGXG	38
7	GTAGXTAXGC	6	56	CGXXTAGTXG	39
8	GGAXGXTAAC	7	57	CXAGGXAAACC	40
9	CXGTATXGTG	8	58	GXGGTTXXTC	68
10	CATXGGTAXG	9	59	CXAGAXGAXG	41
11	GATTXTCGXC	10	60	CGXTGXGTC	42
12	GTTXAXGACC	11	61	CAGXCGTXAG	43
13	CXTCTTXXCC	52	62	GGCTXTGXAC	44
14	CXGAAXGATC	12	63	CXCCGXAATC	69
15	CAAXTACGXC	13	64	GXXACXACAC	70
16	CTCTXAXCCC	53	65	GCXCXGTXC	71
17	CTCXTGGTXC	54	66	GXCXGGAXC	72
18	CGGXATAxAC	14	67	CGAXAGCAXC	73
19	GXAAAXXAGG	15	68	CCCAXTCCXC	74
20	GTCXTAGXXC	16	69	GTGCCXXCAG	75
21	GXCCTXTAXC	17	70	CXCCTAXCGG	76
22	CCXACXTGAG	18	71	GXGTTGXCG	77
23	CTXXCAXAGG	19	72	CXAAGXAXCG	78
24	GXCAAAXCAC	55	73	GGAGXCXXTC	79
25	GTXGAXATGC	20	74	CXGXAXGTAC	80

26	GTTXGCXTTG	56	75	GXACGAXTXG	81
27	GAAAXTGXXG	21	76	GXGCTXCATG	82
28	GCTGXAXATC	22	77	GTGXAGAGXG	83
29	CXCXTXCAAC	57	78	GCCGXCXTC	84
30	CTXXACAXXC	58	79	CAAXCGXTCG	85
31	CXACTCXACC	59	80	CACAXACXGC	86
32	GACXCAXXTG	60	81	CCAGXGXAAG	45
33	CGCAXATXAC	23	82	GGCXAATXGC	46
34	CTCXCTXACG	61	83	GXCTGCXGG	47
35	CTGGXTCXAG	24	84	GXTGGXXCG	87
36	GGAAXAXXCC	25	85	GCCXCCXGT	88
37	GTGGXCTXTC	62	86	CXAXGGTCXC	89
38	CXTCGCXTAC	26	87	CCXXGXGTG	90
39	CAXXACCXAG	63	88	GGXACXCCAG	91
40	GXCXAAAAXG	27	89	GAXCTXCGGC	48
41	GTXCXAXACC	64	90	GCCTXCXGAC	92
42	CXXGACXATC	28	91	GTXCGAXGGG	49
43	CCATXAGXCC	29	92	CXTTXCGXCX	93
44	CACXXTGXTC	65	93	GGXXATCCXG	50
45	GGCAXTXTGG	30	94	CXCTAXGXXG	94
46	CTXAACXGGG	31	95	CXGCXAGXG	95
47	GXTCTXGTC	66	96	CXAGCXACGG	96
48	GGAXACGXG	32	97	GACAXGCXCC	97
49	GCGXTTAXG	33	98	GGGXCGXXA	98

Please replace paragraph [00142] with the following amended paragraph:

[00142] Oligonucleotides were synthesized from natural (A, G, C, and T) nucleotides (Perkin-Elmer/ABI) and isoC, and isoG (EraGen Biosciences, Inc., Madison, WI). The synthesized self-complementary and non-self-complementary sequences are in tables 3 and 4.

**Table 3: Self-Complementary Sequences (Y= iso-G ~~iso-C~~ and X = iso-C ~~iso-G~~)**

3A	GGA CGT CC	Control
3B	GGA YXT CC	Tandem isoC-isoG effect
3C	GXA YXT YC	IsoC-isoG in penultimate position
3D	GGA GCT CC	Control
3E	GGA XYT CC	swapped tandem isoC-isoG effect

**Table 4: Non-Self-Complementary Sequences (Y= iso-G ~~iso-C~~ and X = iso-C ~~iso-G~~)**

4A	SEQ ID NO: 99	5' GCC AGT TTA A 3' 3' CGG TCA AAT T 5'	control
4B	SEQ ID NO:100	5' GCC AXT TTA A 3' 3' CGG TYA AAT T 5'	Single isoC-isoG in AT, TA context
4C	SEQ ID NO:101	5' GCX AGT TTA A 3' 3' CGY TCA AAT T 5'	Single isoC-isoG in mixed GC and AT context
4D	SEQ ID NO: 102	5' GYC AGT TTA A 3' 3' CXG TCA AAT T 5'	Single isoC-isoG in mixed GC and CG context
4E	SEQ ID NO: 103	5' GYY AGT TTA A 3' 3' CXX TCA AAT T 5'	Final tandem isoC-isoG substitution

Please replace paragraph [00152] with the following amended paragraph:

[00152] The resulting thermodynamic parameters determined by Meltwin™ for the self-complementary and non-self-complementary oligonucleotides are summarized in Tables 7 and 8.

**Table 7: Self-Complementary Sequences Thermodynamic Data(~~isoC~~ = Y, ~~isoG~~ = X Y= iso-G and X= iso-C)**

		$-\Delta G_{37}$ (kcal/mol)	$-\Delta H$ (kcal/mol)	$-\Delta S$ (cal/K•mol)	$T_M(^{\circ}\text{C})$ 1.0e-4M
1A	GGA CGT CC	8.27	53.5	145.9	52.8
1B	GGA YXT CC	9.41	57.62	155.4	58.5
1C	GXA CGT YC	10.89	66.27	178.6	63.5
1D	GGA GCT CC	8.10	51.04	138.5	52.4
1E	GGA XYT CC	9.70	57.77	155.0	60.2

**Table 8: Non-Self-Complementary Sequences**  
**Thermodynamic Data (~~isoC = Y~~, ~~isoG = X~~ Y = iso-G and X = iso-C)**

			$-\Delta G_{37}$ (kcal/mol)	$-\Delta H$ (kcal/mol)	$-\Delta S$ (cal/K•mol)	$T_M(^{\circ}\text{C})$ 1.0e-4M
4A	SEQ ID NO:99	5' GCC AGT TTA A 3' 3' CGG TCA AAT T 5'	8.43	69.22	196.0	45.8
4B	SEQ ID NO:100	5' GCC AXT TTA A 3' 3' CGG TYA AAT T 5'	9.56	56.66	151.9	54.5
4C	SEQ ID NO:101	5' GCY AGT TTA A 3' 3' CGX TCA AAT T 5'	9.36	62.98	172.9	51.6
4D	SEQ ID NO:102	5' GYC AGT TTA A 3' 3' CXG TCA AAT T 5'	9.62	54.30	144.1	55.7
4E	SEQ ID NO:103	5' GYY AGT TTA A 3' 3' CXX TCA AAT T 5'	10.59	70.19	192.2	56.0

Please replace paragraph [00154] with the following amended paragraph:

[00154] Tables 7 and 8 show some the extent of the nearest-neighbor effects that are occurring when AEGIS bases are mixed with natural DNA.

**Example 3 and Comparative Example**  
**Site Gated Incorporation**

First primer 5'AGAACCCTTTCCTCTTCC (SEQ ID NO:154)

Target 5'AAGAACCCTTTCCTCTTCCGATGCAGGATACTTAACAATAAATATTT (SEQ ID NO:155)

Second Primer CTACGTCCTATGAATTGTTATTTATAAA~~Y~~XAGGACAGACG 5' (SEQ ID NO:156 )

~~Y~~X = isoCTP

Please replace paragraph [00155] with the following amended paragraph:

[00155] The sequences of the first primer, target, and second primer are shown in SEQ ID NO:~~104~~ 154, SEQ ID NO:~~105~~ 155, and SEQ ID NO:~~106~~ 156, respectively.

Please replace paragraph [00189] with the following amended paragraph:

[00189] The following nucleic acids were used in the multiplex PCR step for this example:

	Sequence	SEQ ID NO
PCR Primer 1A	5' - 6FAM-AGAAACAACCATCTAATCCCACA-3'	<del>113</del> <u>114</u>
PCR Primer 1B	5' - TXCATCTAACAGGGAGCGCC-3'	<del>114</del> <u>157</u>
PCR Primer 2A	5' - 6FAM-CTTCTCCCATTTGCCCAGG-3'	115
PCR Primer 2B	5' - TXTGATGTCTCCACAAAGATCAGTC-3'	<del>116</del> <u>158</u>
PCR Primer 3A	5' - 6FAM-CCTGCAAGCCAGCACC-3'	<del>117</del> <u>118</u>
PCR Primer 3B	5' - TXCCTGCAAGCCAGCACC-3'	<del>118</del> <u>159</u>
PCR Primer 4A	5' - 6FAM-GGTGGAATGTTTGCACATGC-3'	119
PCR Primer 4B	5' - TXGCTGGACCAGGCTAGATAAGC-3'	<del>120</del> <u>160</u>
PCR Primer 5A	5' - 6FAM-CTGATCTGACCTCAGACTGTTG-3'	121
PCR Primer 5B	5' - TXGCAAGGCTCTACTTCCTGC-3'	<del>122</del> <u>161</u>
PCR Primer 6A	5' - 6FAM-GACTGCTGGAGAGCTGAGG-3'	123
PCR Primer 6B	5' - TXGTGTCTTGGCTGCTCAGTATG-3'	<del>124</del> <u>162</u>
PCR Primer 7A	5' - 6FAM-GGACTGTCCAAAGGGATCTC-3'	125
PCR Primer 7B	5' - TXCAACTTCTTGGTCATGGTTGTC-3'	<del>126</del> <u>163</u>
PCR Primer 8A	5' - 6FAM-CAGTATTATCATCTCCTGGCTTAGC-3'	<del>127</del> <u>128</u>
PCR Primer 8B	5' - TXCCTTCCTGCACTCCACAG-3'	<del>128</del> <u>164</u>
PCR Primer 9A	5' - 6FAM-CACATACACCATGTCAGCC-3'	129
PCR Primer 9B	5' - TXTGAGCAGTCGGTCAGTG-3'	<del>130</del> <u>165</u>
Template 1	Mouse genomic DNA; Strain: A/J	
Template 2	Mouse genomic DNA; Strain: C57BL6/J	
Template 3	Mouse genomic DNA; Strain: AB6F1	